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ON THE

MICRO-ORGANISM OF CANCER.

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ALTHOUGH I have left my mind open on the question, I have never believed in the existence of a micro-organism as the cause of cancer until I recently had the opportunity of watching the rapid spread at its edge of a very superficial epithelioma on the vulvar mucous membrane. The activity seemed to be chiefly at the margin of the disease, and its appearance and almost daily invasion of fresh territory convinced me that some infective agency must be at work. The border of the disease was not only brighter in colour than the centre, but it was more raised and appreciable to the touch; the disease, moreover, increased not by the old part growing, but by the invasion of apparently healthy epithelium, which by mere contact became diseased; in fact, it somewhat resembled a ringworm, but was undoubtedly malignant. A second case also confirmed me in the idea of the active operation of a micro-organism; this was a minute rodent ulcer on the cheek with a circular depressed surface, having clear-cut edges or walls. The depressed surface was carefully watched by the patient, a highly intelligent woman, and a powerful hand lens showed that some volcanic action was going on in the little crater. A small

cone would rise on the surface and apparently open at the summit by a minute pore, and discharge something (so she thought), and then subside, the whole cone formation and subsidence occupying one or two days. That this was a small rodent cancer was proved by its microscopic examination after removal. Reflecting upon these cases, and also upon the remarkable discovery by Mr. Haviland that cancer exists endemically in populations living upon low-lying moist soils and in certain "cancer-houses," the conclusion seemed highly probable that the micro-organism must be a fungus, and not, as supposed, a bacterium, coccidium, or protozoon. There is a very large Jewish population in Leeds, probably about 10,000, the female portion of which is constantly seen at the out-patient department of the Leeds Infirmary. In not one Jewess have I ever met with cancer of the genital organs, whereas it is extremely common amongst the Christian women, the inference being (assuming it to be a micro-organism) that it is introduced or not introduced by the husband, according to his faith. Microscopic examination of the secretion frequently contained within the prepuce was the next step, with a very suspicious, but not absolutely certain, result. Some spores were found, and two minute loops of mycelium identical in appearance with that to be described. I have since this examined epitheliomata taken from the ear, the uterus, the breast, the lip, and the penis, and in all five I have without any difficulty demonstrated the existence of a fungus, the same in all cases. (I have also examined a melanotic sarcoma, but the description of this I will leave until later.) The fungus has been seen and examined by a large number of students, qualified residents at the Leeds General Infirmary, medical men in practice, and by some of my own colleagues, and none have had any hesitation in admitting its existence. The mode of preparation is as follows. Whether the preparation is an old one in spirit, or whether it is quite fresh, cut out a very small block from the centre, but in the case of cancer of the lip the free margin should be included. If fresh and not convenient to

examine at once, place in dilute spirit for the night. Next day make as fine sections as possible in the usual way and place them in water. Float off two or three of the best on to slides and drain off as much water as possible. Place upon each three or four drops of liquor potassæ and put them aside protected from dust, to stand for from twenty minutes to four hours, according to the opacity or thickness of the section. When the section appears pretty transparent wash away the liquor potassæ with water without displacing the section. This must be thoroughly done. Then mount in Farrant. If it is merely wished to examine quickly without preservation of the section, put on a drop of liquor potassæ and then the cover-glass. The section will improve for two hours, or if a fresh growth for even four hours, and will then slowly fade. This plan, however, is the best at first, for the idea derived is clearer, as the mycelium comes out gradually and more distinctly and at last but little else is seen. This plan is founded upon the fact that the fungus, with its mycelium, spores, and spore bags, resists the potash longer than the tissues proper. If the action of the potash is not sufficient, the yellow elastic tissue presents a similar appearance to the mycelium. It is, however, larger, coarser, and straighter, and is also sometimes branched, which the mycelium never is. In cancer on the lip it is very important to use the potash long enough. If now the section is held up to the light it will be seen to be very transparent and almost invisible, but here and there small whitish portions are seen. These contain the fungus in the greatest amount. Under a $\frac{1}{9}$ inch objective larger or smaller quantities of extremely fine colourless mycelium are seen. The delicate fibres are rounded, not flat or jointed. They are often contorted and curved so as to form masses of loops. In the epithelioma of the lip the mycelium was especially abundant at the free surface of the sore. It will take no dye, and, indeed, none is required, its great refracting power making it stand out clear and distinct in outline. Any attempt at dyeing makes it all but invisible.

Numerous solitary spores and also the mycelium was found in all the five specimens. In the epithelioma from the auditory meatus (papilloma ?) there were also spore masses not contained in an envelope or wall; these were of irregular shape. In the uterine cancer was seen a spore mass emitting mycelium (see H in drawing). In the

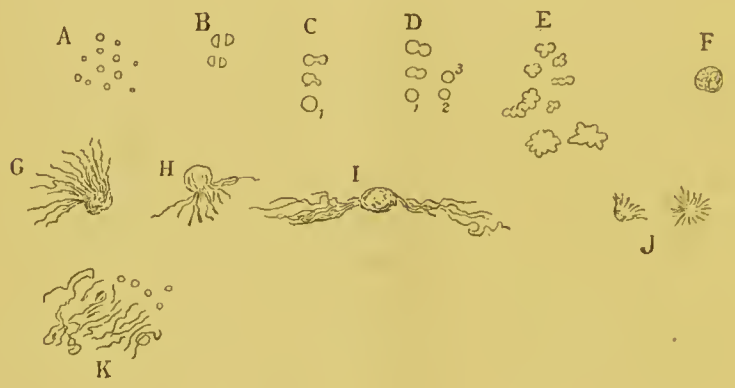

FIG. 1.

A, Primary spores. B, Two spores approach and contiguous sides flatten. C, A tube is projected from one which sucks in the other. D, The commoner mode of conjunction, ending, as does C, in the formation of zygospores (C 1; D 1, 2, 3). E, Conjugation of more than two spores to form spore masses. F, Complete spore mass in envelope or cell membrane; I have called these "spore bags." G, Splitting of spore bag and exit of mycelium. H, Same from the uterine cancer. I, One (the only one seen) emitting mycelium from both ends. J, Spent spore bags. K, Mycelium from the lip cancer at edge of sore.

breast cancer the greater part of the life of the fungus could be studied. This breast had been amputated on May 24, and had been placed in a bowl of water with the tap gently running over it for four days. The disease had not penetrated the skin, which up to the time of operation was intact. One deep incision had been made three-quarters through the large mass. A small block was cut from a part of the tumour about two inches deep. One of the sections happened to contain the fungus alive, and it went through most of its life on the slide (in the Farrant), the hour's immersion in potash not having killed it. Its life in the four or five stages of its existence is as follows.

To begin with, it is a spore mass. This when perfect has a delicate envelope and contains not a number of separate spores, but a fused mass of spores having a granular appearance externally (see F). This spore mass opens or splits at one side and becomes the shape of a shallow tea cup with a wide mouth. From this grows the mycelium, which penetrates in every direction (see G and H). One spore mass only was seen emitting mycelium from both ends (see I); the growth of mycelium could be noted by the eye, but seemed to have ceased on the evening of May 30. The slide was then placed in the cabinet for the night, and next day not a trace of mycelium could be found, but the slide was one mass of spores, which certainly were not there the day before. These were evenly distributed over the slide. I have spent much time in watching these no doubt living spores with intense interest. The process of what is called conjugation had been and was to some extent still going on, until it was stopped by the density of the Farrant's jelly, but the whole process could be seen, and can still, for the slide is yet in good condition. The process appears to be as follows. Two spores approach each other and become flattened at the contiguous sides (see B). From one of these a minute tube soon joins them (see C), and the contents of one spore are sucked into the other, which consequently becomes larger. This would be what is known as a zygospore (see C, 1; D, 1, 2, 3); it is probable that this mode of conjugation only occurs when from some reason the spores cannot actually touch. A commoner mode of conjugation is for two spores actually in contact to become fused into one, all trace of their dual origin vanishing. Similarly, three or four may be so fused, some traces of their compound origin in this case remaining. Not infrequently a considerable number (such as ten or twenty) become fused into one large spore mass (see E). The next step (but this has not been actually seen) is for such a mass to be enclosed in a fine enveloping membrane forming the complete spore bag, with which this description of the life of the fungus began.

When the spore bag is exhausted it presents the appearance as seen at J. The life of the fungus, therefore, seems to consist of four stages—namely, (1) spores; (2) zygospores; (3) spore masses and spore bags; and (4) mycelium which is emitted from the ruptured spore bags. This mycelium gives origin to the spores. This must be the case, but it has not been actually seen.

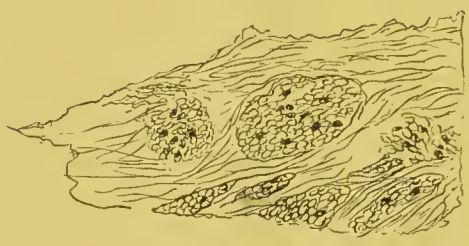

FIG. 2.

Section of melanotic sarcoma, with very low power, showing the spore bags, most of them empty, visible to the naked eye.

To recapitulate, the only parts of the process which have not been actually seen are the formation of the membranous covering of the spore bag, and the formation of the spores in the mycelium. It may be asked, "Have you introduced the fungus by means of the instruments used?" This

FIG. 3.

A few spore bags highly magnified, some empty, with mycelium and spores.

cannot be so, for the fungus in the uterine cancer was found within half an hour of its removal in my own house, and it permeated the whole mass. The epithelioma of the lip was removed by Mr. Mayo Robson at the Leeds General Infirmary on May 30, was in Muller's solution

within half an hour, and was examined next morning. The papilloma of the external auditory meatus was removed by Mr. Secker Walker while I was present at a house within a hundred yards of my own, and was placed in Muller's solution immediately. The epithelioma of the penis was removed at the infirmary by Mr. Walter Brown on May 20, and had been kept from that time in spirit, and was never placed in Muller's solution, so that in all the cases there were different operators and different instruments and different localities, with the exception that two of the specimens came from the infirmary. Examination was made either immediately or next day. The cancer in the breast, however, had been removed four days, and its treatment has been already described. I may now describe the sixth specimen, which had been kept in spirits nineteen months in the pathological room of the infirmary and was labelled "Melanotic Sarcoma." Microscopic examination of this proved the correctness of the title. This was found to be full of mycelium and spores. The mycelium precisely resembled that met with in the epithelioma. Here, however, the resemblance ceased, for there were large masses of spore bags containing as many as 50 to 200 bags each, at least twice the size of the spore bags of epithelioma, and they were egg-shaped instead of round. They readily ruptured, giving exit to the spores, which were of a blackish colour and leaving the empty bags *in situ*. These masses were so large and numerous that they could be seen with the naked eye. It is not likely that this fungus is the same as that of epithelioma assuming another form, as the spores are blackish in colour, and it must be noted that this was not true sarcoma but melanotic sarcoma. No doubt it will be asked whether I assert that this or these micro-organisms are the causes of cancer and sarcoma. No; I do not positively assert this, but I believe it to be the case, for it cannot be a mere accident or coincidence that a fungus was present in every one of the six specimens and in considerable amount. There can be no question

whatever as to its existence, and if any one doubting it could see the sections in my possession, he would be convinced immediately. If anyone would care to refer to the *Transactions of the Obstetrical Society of London* for 1882,[1] he will find the report of a case of non-capsulated fibroid within the uterus, in which a fungus was found by me in a large amount, but it was not the same fungus as that of epithelioma or that of melanotic sarcoma, so that this discovery to a certain extent naturally sprang out of that. I have also lately found a few spores, but no mycelium in the growing base of a mucous polypus of the cervix uteri, also in that of a fibroid polypus, and in a uterine fibroid weighing ten pounds, which I removed a short time ago by abdominal section. These may have been accidentally introduced, but in the mucous polypus they seemed to be regularly arranged in the tissues. I will therefore hazard the conjecture, but it is a mere guess, that many other forms of tumour will be found to have a fungoid origin. In this case the theory which I published a few years ago in the *Lancet*[2] will explain why some of them are malignant and some are not, and just as it appears probable that one fungus affects only epithelium and causes true cancer, and that another affects only mesoplastic tissues and produces sarcoma, so it will be found that each form of tumour has its own fungus. It is probable that the fungus of ordinary sarcoma is not exactly identical with that described in the account of the specimen of melanotic sarcoma. Much, of course, is yet wanting to prove the case absolutely, but the cultivation of the fungus under direct observation in Farrant is very easy, and probably it would be easier still in some form of jelly containing no antiseptic and of more fluid consistence, so as to allow of movement of the spores. It is almost evident that the primary spores are sterile, also no mycelium has been seen to emanate from zygospores, but

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[1] Vol. xxii., p. 182.

[2] The *Lancet*, June 30, 1888.

they are presumably fertile under some condition or other. The spore bags are undoubtedly very fertile, and must be present so far as can be seen at present for any successful cultivation. It is also not unlikely that mycelium in order to produce spores must maintain its connexion with its nourishing spore bag, and if so mycelium alone would be sterile.

Next arises the natural question, Is any practical result likely to result from this discovery if it should prove after the careful investigation it will doubtless receive that it is the real explanation of the cause of malignant growth? So far as I can see at present the answer may be given as follows: (1) The cure of a cancerous growth actually in existence does not seem more probable but less probable, because the enemy is so subtle, so penetrating, and so indestructible (proved by immersion in liquor potassæ for an hour not killing it) that it almost seems impossible to eradicate it; it is, however, better to have an enemy exposed to view than one invisible. But it seems likely that after removal of a growth by operation it would be better not to close the wound absolutely, but to keep the surface in contact with dressings soaked in glycerine containing liquefied carbolic acid and also perchloride of mercury (the carbolic acid partly to relieve pain). Glycerine penetrates tissues and carries with it any substance in solution. (2) It seems not improbable that cancer of the breast may be altogether prevented in women past the child-bearing period by merely closing the orifices of the milk ducts in the nipple by a small surgical operation, or by the use of a fine electric cautery, for the fungus must enter the breast *viâ* the milk duct orifices. (3) It is possible that we may have to return to a certain Mosaic rite in order to save our wives from uterine cancer, unless the daily use of soap will do away with this necessity. (4) In order to prevent the fearful mortality from cancer in low-lying wet soil districts the bodies of persons dying from cancer must be specially buried at a great depth or they must be cremated. It will be seen that moisture is absolutely

necessary for the formation of zygospores, spore masses, and spore-bearing mycelium. It does not seem probable that the fungus necessarily spends part of its life in the earth, but no doubt when the interment is at no great depth the earth will become infiltrated, if it is constantly wet, and floods will carry the spore masses all over the country. (5) A fungus can only attack effete tissues. We are ourselves only tools of nature; we must keep ourselves bright by constant use; we must not rust from luxury and idleness. Business men must be careful how they retire, for just as tuberculosis is favoured by excessive work and poor food, so the growth of a fungus is likely to be favoured by the effete materials present in the system engendered by the opposite conditions. We cannot, however, foretell what may be the result of this discovery, if discovery it is. Some remedy may be found which will destroy the fungus. I will now leave the matter to the judgment of my professional brethren. It is certain to excite great interest and many divergent opinions, for is not cancer the most terrible scourge to the human race which exists? The mere dread of it has been known to unhinge the mind, increasing as it is in frequency, and producing an amount of misery which no pen can describe.

Addendum.—Since this paper was written I have, by means of an able working pathologist who has been engaged for several years in a small pathological laboratory in my own house, made over 150 slide preparations of malignant and other healthy (?) and diseased tissue, and have come upon unexpected and startling results, which not only confirm most of what is already published in this paper—for in not one primary malignant case was the fungus absent—but render it highly probable that other diseases, and amongst them diabetes, are caused by fungi. I have also worked out rather more completely the life-history of the fungi of epithelioma and of sarcoma, and propose, with the kind permission of the editors of the *Lancet*, to describe these further results in a subsequent paper. Meanwhile, and until this is done, I shall be grateful if criticism is with-

held. It is extremely easy for anyone to satisfy himself as to the existence of the fungi, and it would be better for actual investigation to precede criticism.

Since the preceding article was published in the *Lancet* of June 27 last, I have examined a greater number of primary malignant growths, altogether nearly forty in number. No less than eight or possibly nine different fungi have been differentiated as occurring in the various forms of cancer. These can be distinguished from one another by peculiarities in the mode of formation of the spores, or by the appearance and life-history of the spores themselves, or by peculiarities of the mycelium. Each form of malignant disease appears to have its own peculiar fungus, and I will almost undertake to tell what form of cancer is presented to me by the fungus which it contains.

A second paper was sent to the editors of the *Lancet*, giving full particulars, and accompanied by illustrations, but the editors wrote to say the subject was so important that they thought it better before publication it should be brought before some medical society in order that the slides might be examined by competent pathologists, and the subject fully discussed. No better opportunity can be offered for this than a meeting of the British Medical Association, and it is hoped that time will be found for discussion. As the length of the paper is limited to fifteen minutes, it cannot, however, give quite as full details as I should wish.

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